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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/841,580	04/24/2001	Andrea Califano	YOR920000687US2	5406

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EXAMINER

CLOW, LORI A

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 12/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/841,580	<b>Applicant(s)</b> CALIFANO ET AL.	
	<b>Examiner</b> Lori A. Clow, Ph.D.	<b>Art Unit</b> 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 04 October 2004.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-3, 17-19 and 23-25 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3, 17-19, and 23-25 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

Applicants' response, filed 4 October 2004, has been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 1-3, 17-19, and 23-25 are currently pending.

#### **Claim Rejections - 35 USC § 101**

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-3, 17-19, and 23-25 remain rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility.

Applicant provides no arguments with regard to the outstanding utility rejection except that amendments have been made for clarity. The Examiner maintains that the claimed method is merely directed to transforming data that represent gene expression signals. The specification, however, does not teach any utility for a method that simply transforms expression signal data by itself. Use of the claimed method to analyze the expression signals such that patterns are identified is certainly of scientific interest; however, no specific, substantial, and credible utility is set forth for the mere transformation of data.

A putative use is now recited, however the result of the data transformation is still not known. What does one do with transformed data? What is the result of the transformation process? The

claimed method still simply converts signals to a uniform distribution, without any further steps such that the result is "immediately useful" to one of skill in the art.

Claims 1-3, 17-19, and 23-25 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either an asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

#### **Claim Rejections - 35 USC § 112-1st Paragraph**

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 17-19, and 23-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands* (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

a) In order to practice the claimed invention one of skill in the art must be able to transform data that transforms gene expression signals. For the reasons discussed below, this constitutes undue experimentation.

b) and c) The specification at page 4, beginning line 20, states the following, for example:

“Generally, the present invention applies a transformation to convert a probability distribution of gene expression signals in control samples to a uniform distribution. The uniform distribution allows better comparisons between expression levels for genes. The transformation is derived from gene expression signals of control data and is applied to gene expression signals of phenotype data. The phenotype data can be represented in a matrix format. A number of gene expression patterns may be determined (in the form of submatrices) that will characterize the phenotype. The uniform distribution helps in this regard as it allows better comparisons of patterns. The gene expression patterns can then be used to classify samples as belonging to the phenotype set”.

The specification does not teach how to derive a transformation that transforms gene expression signals. Instead, as recited about, the specification teaches applying a transformation to convert a probability distribution of gene expression signals in control samples to a uniform distribution. The uniform distribution is then used for the comparison of expression levels in genes.

Further, the specification teaches the following at page 6, beginning line 21:

“Basically, the present invention is used to take an initial set of expression data for one phenotype (generally called the control set and containing information from healthy cells) and to determine transformations from this data. The transformations are applied to a set of expression data from another phenotype (generally called the phenotype set and containing information from unhealthy cells). The transformed set of data is used to determine gene expression patterns that are characteristic of the phenotype. New expression data from samples that have an unknown genetic makeup are compared with the gene expression patterns”.

Art Unit: 1631

The instant claims are not drawn to comparison of any control transformation for phenotypes or comparison with unhealthy cells to determine gene expression patterns. It is unclear in the instant claims how one is to use a function to create a transformation or how a uniform distribution is converted by the transformation. The instant specification sheds no light on how to perform such a method.

d) The claims are drawn to a method for transforming gene expression signals by somehow deriving a transformation that transforms the plurality of gene expression signals into a uniform distribution which is then used to determine gene expression signals.

e) and g) The prior art does not teach transforming gene expression signals and using a uniform distribution for the determination of gene expression signals.

f) The skill of those in the art of bioinformatics is high.

h) The claims are not commensurate in scope with the specification for the reasons stated above. The skilled practitioner would first turn to the instant specification for guidance to practice methods. However, the instant specification does not provide specific guidance to practice these embodiments. As such, the skilled practitioner would turn to the prior art for such guidance, however, the prior art does not teach such a method. Finally, said practitioner would turn to trial and error experimentation. Such represents undue experimentation

#### **Claim Rejections - 35 USC § 112-2<sup>nd</sup> Paragraph**

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 17-19, and 23-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 17, and 23 recite a step of “deriving a transformation that transforms, within a selected interval”. It is unclear what interval is intended for selection. Is the interval one of time, space, gene location, level of expression or some other interval? Clarification is requested.

Claims 1, 17, and 23 recite “deriving a transformation that transforms”. However, it is unclear what transformation is taking place. What is being transformed; signal intensity, width of the peak, area under a curve or some other parameter? Clarification is requested.

Claims 1, 17, and 23 recite “deriving a transformation that transforms [...] gene expression signals into a uniform distribution of transformed gene expression [...] each gene expression signal is converted by the transformation into a transformed gene expression signal in the uniform distribution”. It is unclear what is intended by this step of the claim, as it is a circular step and thus confusing. Clarification is requested.

### **Conclusion**

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after

Art Unit: 1631

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

In view of the new limitations set forth in claims 1, 17, and 23, which explicitly recite the "transformation of data", the non-statutory rejection under 35 USC 101 has been withdrawn.

In view of the amendments to the claims reciting "transformation that transforms", the rejection under 35 USC 112, 1<sup>st</sup> paragraph (New Matter) has been withdrawn.

### Inquiries

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The Central Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (571) 272-0715. The examiner can normally be reached on Monday-Friday from 10 am to 6:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward, Ph.D., can be reached on (571) 272-0722.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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December 15, 2004  
Lori A. Clow, Ph.D.  
Art Unit 1631

*Lori A. Clow*

*12/16/04*  
MARJORIE MORAN  
PATENT EXAMINER